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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,436	03/21/2002	Zoltan Greff	22096	6522

535 7590 06/11/2004

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EXAMINER	
COLEMAN, BRENDA LIBBY	
ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 06/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/030,436	GREFF ET AL.	
	Examiner	Art Unit	
	Brenda Coleman	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-27 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-27 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-27 are pending in the application.

Priority

1. It is noted that this application appears to claim subject matter disclosed in prior Application No. PCT/HU00/00074, filed July 4, 2000. A reference to the prior application must be inserted as the first sentence of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e) or 120. See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. Also, the current status of all nonprovisional parent applications referenced should be included.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This

time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 16-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for epilepsy, does not reasonably provide enablement for "neuroprotective effect" and/or "neurodegenerative diseases". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in

scope with these claims. The scope of "neurodegenerative disease" cannot be deemed enabled. The term "neurodegenerative disease" covers a broad array of different disorders that have different modes of action and different origins. The term covers such diverse disorders as Alzheimer's Disease; Parkinson's Disease; ALS and variants such as forms of ALS-PDC; Gerstmann-Straussler-Scheinker Disease (GSS); Pick's Disease; Diffuse Lewy Body Disease; Hallervordon-Spatz disease; progressive familiar myoclonic epilepsy; Corticodentatonigral degeneration; progressive supranuclear palsy (Steele-Richardson-Olszewski); Huntington's disease; more than a dozen dementias collectively called "frontotemporal dementia and Parkinsonism linked to chromosome 17" (FTDP-17); Tourette's syndrome; Shy-Drager syndrome; Friedrich's ataxia and other spinocerebellar degenerations; Olivopontocerebellar atrophy (OPCA); spasmotic torticollis; Striatonigral degeneration; various types of torsion dystonia; certain spinal muscular atrophies, such as Werdnig-Hoffmann and Wohlfart-Kugelberg-Welander; Hereditary spastic paraplegia, Primary lateral sclerosis; peroneal muscular atrophy (Charcot-Marie-Tooth); Creutzfeldt-Jakob Disease (CJD); Hypertrophic interstitial polyneuropathy (Dejerine-Sottas); retinitis pigmentosa; Leber's Disease; and Hypertrophic interstitial polyneuropathy. These exhibit a very broad range of effects and origins. For example, some give progressive dementia without other prominent neurological signs, such as Alzheimer's disease, whereas other dementias have such signs, such as Diffuse Lewy Body Disease. Some give muscular wasting without sensory changes, e.g. ALS, and some do have the sensory changes such as Werdnig-Hoffmann. Some are abnormalities of posture, movement or speech, such as

Striatonigral degeneration, and other are progressive ataxias, such as OPCA. Some are linked to tau mutations, such as Alzheimer's disease and FTDP-17, and other such as Parkinson's clearly do not. Some affect only vision such as retinitis pigmentosa. Even within those that fall into the same category of effects, there are often striking differences. For example, Alzheimer's disease and Pick's disease both give progressive dementia without other prominent neurological signs. But the characteristic Alzheimer's neurofibrillary tangles are not seen in Pick's Disease, which has straight fibrils, as opposed to the paired helical filaments of Alzheimer's disease. Pick's Disease gives lobal atrophy, not seen in Alzheimer's disease. There are differences in origins, even with what little is known. Thus, among progressive dementias, CJD is definitely caused by an infectious agent; so far as can be determined, this is not so for Huntington's disease. Even among the hereditary disorders, the origins are different. Thus, FTDP-17 comes from chromosome 17, Huntington's disease from 4, and the neurodegenerative disorder that people with Down's syndrome develop later in life is presumably connected in some way to 21.

The great majority of these have no treatment at all, and of those that do, none or virtually none have been treated with such inhibitors as are disclosed here. The great diversity of diseases falling within the "neurodegenerative disease" category means that it is contrary to medical understanding that any agent (let alone a genus of trillions of compounds) could be generally effective against such diseases. The intractability of these disorders is clear evidence that the skill level in this art is low relative to the difficulty of the task. Further, what little success there has been does not point in this

direction. Thus, what very few treatments that the massive research effort on Alzheimer's disease has produced are means of providing Acetylcholinesterase inhibition, unrelated to the mechanism of action in this case.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

3. Claims 1-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a) Claims 1-4, 6, 12, 13, 16-19 and 25-27 (and claims dependent thereon) are vague and indefinite in that it is not known what is meant by "compounds of the general Formula. A formula is not general when all of the variables are defined. Deletion of "general" is suggested.

b) Claim 12 and claims dependent thereon are vague and indefinite in that it is not known what is meant by the process of preparation of compounds of the general Formula I. There is no Formula I in independent claim 12.

c) Claim 12 and claims dependent thereon recite the limitation "-C(=O)-NR^7R^8" in the structure of Formula VI where the -C(=O)-NR^7R^8 moiety is attached to C8. There is insufficient antecedent basis for this limitation in the claim.

d) Claim 16 and claims dependent thereon are vague and indefinite in that it is not known what is meant by the pharmaceutical composition, which comprises

as active ingredient a compound of the general Formula I. There is no Formula I in independent claim 16.

e) Claim 17 and claims dependent thereon are vague and indefinite in that it is not known what is meant by Formula I, which is not present in this dependent claim or the claim from which it depends.

f) Claims 18 and 19 and claims dependent thereon recite the limitation "Formula IB" in the composition of these claims. There is insufficient antecedent basis for this limitation in the claim.

g) Claim 24 is vague and indefinite in that it is not known what is meant by this independent claim, which contains no formula.

h) Claim 24 is a substantial duplicate of claims16-23 as the only difference is a statement of intended use, which is not given material weight. Note In re Tuominen 213 USPQ 89.

i) Claim 26 provides for the use of the compounds of general Formula I, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

j) Claims 24 and 26 and claims dependent thereon are vague and indefinite in that it is not known what is meant by vomitting or schisophreny.

k) Claim 26 and claims dependent thereon are vague and indefinite in that it is not known what is meant by the process of preparation of compounds of the general Formula I. There is no Formula I in independent claim 26.

l) Claim 27 is vague and indefinite in that it is not known what is meant by the process of preparation of compounds of the general Formula I. There is no Formula I in independent claim 27.

m) Claims 26 and 27 are vague and indefinite in that it is not known what is meant by "especially Parkinson disease, Alzheimer disease, amyotropic lateral sclerosis, stroke, acute head injuries, epilepsy, against spasms, alleviation of pain, to influence vomiting, schisophreny, migraine, urination problems, as anxyolitics, against drug addiction and to alleviate the symptoms of Parkinsonism". It is not known what else is being contemplated.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claim 26 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1, 2, 4, 5, 10-13, 16, 17 and 22-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hamori et al., U.S. 5,756,495. The generic structure of Hamori encompasses the instantly claimed compounds (see Formula I, column 1 and Formula II, column 4) and by the same process and uses as claimed herein. Examples 1-3, 6, 7, 14, 20-43 and 45-53 differ only in the nature of the R^1 and R^2 substituents. Column 1, lines 33-35 defines the substituents R^1 and R^2 as the same or different and mean hydrogen, C_1-C_6 alkyl, nitro, halogen, the group $-NR^8R^9$, -O-C_{1-4} alkyl or $-CF_3$. The compounds of the instant invention are generically embraced by Hamori in view of the interchange ability of the R^1 and R^2 substituents of the tricyclic ring system. Thus, one of ordinary skill in the art at the time the invention was made would have been motivated to select for example R^2 is methyl and R^1 is nitro and amino as well as other possibilities from the generically disclosed alternatives of the reference and in so doing obtain the instant compounds in view of the equivalency teachings outlined above.

6. Claims 1, 2, 4, 5, 10-13, 16, 17 and 22-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hamori et al., U.S. Patent No. 5,756,495. The prior art generically teaches the compounds that are structural homologs of the compounds as

claimed herein, i.e., they differ by a methyl group. The instant compounds are structural homologs of the reference compounds where on the instant compounds the substituent at the 3-position of the phenyl ring is a methyl group, whereas the reference teaches a H atom at the 3-position of the phenyl ring. The reference's examples 1-3, 6, 7, 20-43 and 45-53, differ from the claimed invention only in the nature of the substituent on the 3-position of the phenyl ring system, i.e. H vs. Me. 4-amino-3-methylphenyl and 3-methyl-4-nitrophenyl are not patentably distinct from the 4-aminophenyl and 4-nitrophenyl ring systems in the prior art since the only difference is H vs. Me. H vs. Me is not deemed patentably distinct absent evidence of superior or unexpected properties. See In re Wood 199 USPQ 137; In re Lohr 137 USPQ 548 regarding the addition of a Me group to a known compound. Furthermore, applicants should note a replacement of two methyl groups on a known compound with two hydrogen atoms has been held to be prima facie obvious due to close structural similarity. Note In re Hoke, 195 USPQ 148 and Ex parte Fauque, 121 USPQ 425. Thus, one having ordinary skill in the art would have been motivated to prepare the instantly claimed invention because such structurally homologous compounds are expected to possess similar properties.

Conclusion

7. U.S. Patent No. 5,756,495 claims subject matter that is similar and/or identical to that claimed herein. Two patents cannot issue on the same subject matter, unless applicants can demonstrate that the claims are patentably distinct from the claims of this US patent, the only way to overcome this patent is by way of Interference proceedings or removal of the conflicting subject matter. See MPEP 2306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 571-272-0674. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brenda Coleman

Brenda Coleman
Primary Examiner Art Unit 1624
June 8, 2004